

CLAIMS

What we claim is:

1. A multi-valent immunogenic composition for conferring protection in a host against disease caused by both *Haemophilus influenzae* and *Moraxella catarrhalis*, which comprises:

at least four different antigens comprising at least one antigen from *Haemophilus influenzae* and at least one antigen from *Moraxella catarrhalis*, at least three of which antigens are adhesins and at least one of which adhesins is from *Moraxella catarrhalis*.

2. The immunogenic composition of claim 1 wherein one of said antigens which is an adhesin is a high molecular weight (HMW) protein of a non-typeable strain of *Haemophilus influenzae*.

3. The immunogenic composition of claim 2 wherein said HMW protein is a HMW1 or HMW2 protein of the non-typeable strain of *Haemophilus influenzae*.

4. The immunogenic composition of claim 1 wherein another of the antigens which is an adhesin is a *Haemophilus influenzae* adhesin (Hia) protein of a non-typeable strain of *Haemophilus influenzae* or a *Haemophilus influenzae* surface fibril (Hsf) protein of a typeable strain of *Haemophilus influenzae*.

5. The immunogenic composition of claim 1 wherein an antigen of *Haemophilus influenzae* which is not an adhesin is a non-proteolytic heat shock protein of a strain of *Haemophilus influenzae*.

6. The immunogenic composition of claim 5 wherein the non-proteolytic heat shock protein of a strain of *Haemophilus influenzae* is an analog of *Haemophilus influenzae* Hin47 protein having a decreased protease activity which is less than about 10% of that of natural Hin47 protein.

7. The immunogenic composition of claim 1 wherein one of said antigens which is an adhesin is an outer membrane protein of *Moraxella catarrhalis* having an apparent molecular mass of about 200 kDa, as determined by SDS-PAGE.

8. A multi-valent immunogenic composition for conferring protection in a host against disease caused by both *Haemophilus influenzae* and *Moraxella catarrhalis*, which comprises:

(a) an analog of *Haemophilus influenzae* Hin47 protein having a decreased protease activity which is less than about 10% of natural Hin47 protein,

(b) a *Haemophilus influenzae* adhesin (Hia) protein of a non-typeable strain of *Haemophilus influenzae*,

(c) a high molecular weight (HMW) protein of a strain of non-typeable *Haemophilus influenzae*, and

(d) an outer membrane protein of *Moraxella catarrhalis* having an apparent molecular mass of about 200 kDa, as determined by SDS-PAGE.

9. The composition of claim 8 wherein said Hin47, Hia, HMW and 200 kDa proteins are present in amounts which do not impair the individual immunogenicities of the proteins.

10. The composition of claim 9 wherein said analog of Hin47 protein is one in which at least one amino acid of the natural Hin47 protein contributing to protease activity has been deleted or replaced by a different amino acid and which has substantially the same immunogenic properties as natural Hin47 protein.

11. The composition of claim 10 wherein said at least one amino acid is selected from the group consisting of amino acids 91, 121 and 195 to 201 of natural Hin47 protein.

12. The composition of claim 11 wherein Serine-197 is replaced by alanine.

13. The composition of claim 11 wherein Histidine-91 is replaced by alanine, lysine or arginine.

14. The composition of claim 13 wherein Histidine-91 is replaced alanine.

15. The composition of claim 11 wherein Asp-121 is replaced by alanine.

16. The composition of claim 9 wherein said Hia protein is produced recombinantly.

17. The composition of claim 16 wherein said recombinantly-produced Hia protein is an N-terminal truncation V38 rHia.

18. The composition of claim 9 wherein said HMW protein is an HMW1 or HMW2 protein of a non-typeable strain of *Haemophilus influenzae*.

19. The composition of claim 18 wherein the HMW1 and HMW2 proteins are produced recombinantly.

20. The composition of claim 19 wherein said HMW1 and HMW2 proteins are derived from the respective strain of non-typeable *Haemophilus influenzae* and possess respective molecular weights as set forth in the following Table:

<u>Molecular Weight (kDa) non-typeable <i>H.influenzae</i> Strain</u>							
		12	JoyC	K21	LCDC2	PMH1	15
Mature Protein:	HMW1	125	125.9	104.4	114.0	102.4	103.5
	HMW2	120	100.9		111.7	103.9	121.9

21. The composition of claim 9 wherein said 200 kDa protein is produced recombinantly.

22. The composition of claim 21 wherein recombinantly-produced 200 kDa protein is an N-terminal truncation V56 r200 kDa.

23. The composition of claim 8 further comprising an adjuvant.

24. The composition of claim 23 wherein said adjuvant is aluminum hydroxide or aluminum phosphate.

25. The composition of claim 8 comprising

- (a) about 25 to about 100 µg of the Hin47 protein analog, and
- (b) about 25 to about 100 µg of the Hia protein,
- (c) about 25 to about 100 µg of the HMW protein, and
- (d) about 25 to about 100 µg of the 200 kDa protein.

26. The composition of claim 8 further comprising at least one additional antigenic component for conferring protection against infection caused by another pathogen.

27. The composition of claim 8 wherein said at least one additional antigenic component is selected from the group consisting of diphtheria toxoid, tetanus toxoid, pertussis antigens, non-virulent poliovirus and PRP-T.

28. The composition of claim 27 wherein said pertussis antigens are selected from the group consisting of pertussis toxoid, filamentous hemagglutinin, pertactin and agglutinogens.

29. A method of immunizing a host against disease caused by infection with both *Haemophilus influenzae* and *Moraxella catarrhalis*, including otitis media,

which comprises administering to the host an immunoeffective amount of a composition as claimed in claim 1 or 8.